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Ottawa Hull K1A 0C9

(21) (A1) 2,164,766
(22) 1995/12/08
(43) 1996/06/11

(51) Int.Cl. ⁶ C12N 7/06; A61L 2/18; A61K 35/12

(19) (CA) **APPLICATION FOR CANADIAN PATENT** (12)

(54) Process for the Inactivation of Viruses with the Aid of
Acridine or Acridine Derivatives

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(30) (DE) P 44 44 045.6 1994/12/10

(57) 14 Claims

Notice: This application is as filed and may therefore contain an
incomplete specification.



5 Process for the inactivation of viruses with the aid of
acridine or acridine derivatives

10 The invention relates to the use of acridine or acridine
derivatives, preferably in combination with benzalkonium
chloride, for the inactivation of enveloped or nonenvelo-
ped viruses. The process according to the invention is
preferably carried out in the presence of proteins whose
biological activity is largely retained.

15

It has been known for years that untreated human plasma
or serum can contain human pathogenic viruses, such as
HIV, HBV or HCV, which, if transmitted to sensitive
recipients, can cause serious diseases, such as AIDS or
20 hepatitis. In order to prevent this potential virus
transmission, therapeutics which are obtained from human
plasma or serum are prepared, on the one hand, only from
preselected starting materials which, as far as anyone
can judge, are virus-free and, on the other hand, are
25 subjected to virus-inactivating/eliminating steps in the
preparation process. The efficiency of the virus inacti-
vation/elimination method used is established using
strict measures and continuously checked.

30 Besides physical virus inactivation steps, chemical virus
inactivation steps are also known in the preparation of
said therapeutics. A particularly frequently discussed
chemical process is the SD (solvent/detergent) method. It
is suitable for inactivating enveloped viruses, i.e.
35 viruses which are surrounded by a lipid-containing
membrane, but has the crucial disadvantage of being
completely ineffective against all known nonenveloped
(uncoated) viruses. Moreover, also no other chemical
process is known which would be suitable to inactivate

nonenveloped viruses while simultaneously retaining the biological activity of the protein constituents of the therapeutic or of the human plasma or serum.

- 5 Although the chemical virus inactivation processes are only used in a supplementary capacity to the physical methods, and although most viruses potentially transmissible by blood and blood products carry a lipid coat, for reasons of safety there is an exceptional need to make
10 available chemical inactivation processes which also reliably inactivate nonenveloped viruses. This is all the more desirable as recently also HAV and parvoviruses, for example parvovirus B 19, were discussed as viruses which are potentially transmissible by blood fluids or blood
15 products. (Vox Sanguinis 67, Supplement 1, 1994: Proceedings of a Symposium held at the New York Blood Center).

The invention was also based on the object of developing an industrially utilizable process for chemical virus
20 inactivation, in which enveloped and nonenveloped viruses, e.g. parvoviruses, are inactivated with retention of the biological activity of proteins present, e.g. therapeutically useful proteins.

- 25 This object is achieved according to the invention by adding acridine or an acridine derivative to the protein-containing liquid to be treated. It was surprisingly found that acridine or acridine derivatives inactivate enveloped and nonenveloped viruses. Acridine derivatives
30 are, for example, ethacridine, 9-aminoacridine (=aminacrine), 3,6-acridinediamine (proflavine), acrisorcin, Acrizane chloride (=phenacridane chloride), Acridine Orange, quinacrine, acricide, acridone, acridine-9-carboxylic acid, acranil (1-[(6-chloro-2-methoxy-9-acridinyl)amino]-3-(diethylamino)-2-propanol dihydrochloride),
35 3,7-diamino-5-phenylphenazinium chloride (phenosafranin, Safranin B Extra), phenoxazine, phenothiazine and especially acriflavine (3,6-diamino-10-methylacridinium chloride and 3,6-acridinediamine) and

their salts, e.g. chlorides, sulfates, bromides.

Surprisingly, it was additionally found that a combination of acridine or an acridine derivative and benzalkonium chloride displays a synergistic action during virus inactivation; i.e. the magnitude of the virus inactivation of the combination is higher than that of each individual substance.

- 10 The virus inactivation process according to the invention can be carried out with protein solutions such as blood, serum, plasma, blood products, allantoic fluid or milk. The virus inactivation is carried out at a pH of 3 to 10 or 5 to 9 (in, for example, serum or plasma solutions)
- 15 and a temperature of 1°C to 80°C, preferably of 20°C to 60°C, very preferably from 20°C to 40°C, or 25°C to 37°C, and lasts 30 minutes to 10 hours, preferably 2 to 5 hours. For virus inactivation, a concentration of 1.0 g/l - 0.00001 g/l or 1.0 g/l - 0.004 g/l, preferably
- 20 0.1 g/l-0.001 g/l, is used for the acridines or acridine derivatives, and a concentration of 0.1 g/l - 0.004 g/l, preferably 0.05 g/l - 0.01 g/l, for benzalkonium chloride.
- 25 The removal of the acridines and of the benzalkonium chloride from the protein solutions, if this is necessary, is possible by means of simple, known methods, such as adsorption on active carbon or dialysis.
- 30 A further advantage of the virus inactivation process according to the invention is the very extensive protection of the protein constituents of the material to be treated: different biological activities, e.g. antibody activity and clotting activity, are not reduced or only
- 35 reduced to a tolerable extent.

The virus inactivation process according to the invention can therefore be employed, for example, for the decontamination of the following materials:

- protein-containing solutions (dilute or concentrated)
- blood or blood products; both the liquid and the cellular constituents
- 5 - serum, plasma
- allantoic fluid
- organ extracts
- milk
- buffer solutions
- 10 - antigens for diagnostics
- vaccines, antigens for vaccines

The process according to the invention is furthermore suitable for disinfection in virus contamination of, for example, areas, equipment, effluents, wastes and surfaces of all types. The disinfection of virus-contaminated organ transplants, e.g. cornea, cerebral meninges, liver, heart, lungs or kidneys is also possible.

20 The present invention is furthermore illustrated by the following examples.

Methods generally used in the process according to the invention

25 Virus: Was replicated in a known manner in tissue cultures; the virus harvests were centrifuged and used as starting material for the further investigations.

The infectiousness titer was determined in microtiter plates - 8 replicates of 0.1 ml/- dilution stage - by double titration.

Stock	Ethacridine	3% strength	
solu-	lactate (EL)	in dist. water)	
tions:	Entozon® (E)	3% strength	Acridines
		in dist. water}	
	Acriflavine (A)	1% strength	
		in dist. water)	

Benzalkonium 10% in dist.
chloride (BACI) water

General experimental procedure:

9 parts of buffer or medium or protein solutions were
5 mixed with 1 part of virus. The addition of the amounts
of the stock solutions indicated in the individual
examples for virus inactivation and renewed mixing with
subsequent virus titration were then carried out. After
the times and temperatures mentioned in the individual
10 examples, samples were removed and titrated in double
determinations in order to be able to measure the
process-related virus inactivation.

Types of virus investigated

15	Abbreviation	Name
	PI ₃ V	Bovine parainfluenza 3 virus
	BPV	Bovine parvovirus
	PPV	Porcine parvovirus
	IBRV	Infectious bovine rhinotracheitis
20		virus
	BVDV	Bovine viral diarrhoea virus
	CPV	Canine parvovirus
	BAV-1	Bovine adenovirus type 1
	Reo 3	Reovirus type 3
25	Influenza A	Influenza A virus-Shangdong
	Influenza B	Influenza B virus - B Panama

Further abbreviations/names used in the text:

30	EME Medium	Eagles Minimum Essential Medium
	Beriate®P	Clotting factor VIII:C concentrate, pasteurized (Behringwerke AG, Marburg, Germany)

- Haemate®P Concentrate from clotting factor VIII and Von-Willebrand factor, pasteurized (Behringwerke AG, Marburg, Germany)
- Beriplex®P Pasteurized prothrombin complex concentrate (Behringwerke AG, Marburg, Germany)
- Venimmun® Human polyvalent immunoglobulin preparation (7S) for intravenous use (Behringwerke AG, Marburg, Germany)
- Entozon® Preparation of the following composition:
1 g of granules contains 0.059 g of dimethoxy-6-nitro-9-[(3-diethylamino-2-hydroxy)propylamino]acridine dihydrochloride and 0.295 g of ethacridine lactate (ASID Veterinär Vertriebs GmbH)
- 5 QAE cellulose Diethyl-2-hydroxypropylaminoethyl cellulose
(Ion exchanger for protein purification)
- FCS Fetal calf serum

Example 1

10 Inactivation of PI₃V by BACI

EME medium was mixed with PI₃ virus and BACI and incubated at 37°C in a water bath. After the times indicated, samples were taken to test for virus inactivation. The results are shown in Tab. 1.

Table 1Inactivation of PI₃ virus with BACI at 37°C

Time (h)	BACI addition (mg/ml)	Virus titer found (log ₁₀ /ml)	Virus inactivation (log ₁₀ /ml)
5	0 (control)	7.4	-
	0.1	≤1.5	≥5.9
	0.005	≤1.5	≥5.9
	0.025	6.0	1.4
	0.0125	6.9	0.5
10	0 (control)	6.8	-
	0.1	≤1.5	≥5.3
	0.05	≤1.5	≥5.3
	0.025	≤1.5	≥5.3
	0.0125	5.5	1.3

¹⁾ Identical after addition of BACI and thorough mixing of the reaction batch

20 As emerges from the results in Table 1, PI₃ virus is very rapidly inactivated by the high doses of BACI (0.1 mg/ml, 0.05 mg/ml), i.e. in the time which was needed to mix the virus-containing sample thoroughly with BACI, to take a sample and to titrate this in order to determine the infectiousness of PI₃ virus, infectious virus was no longer detectable. At the two other BACI concentrations tested (0.025 mg/ml and 0.0125 mg/ml), a clear concentration-time dependence of virus inactivation is discernible.

30

Example 2

Virus inactivation by means of BACI or Entozon

35 The virus species shown in Tab. 2 were treated with BACI or Entozon and incubated at 45°C. Sample taking for virus titration was carried out 1 or 2 hours after the start of the test.

Table 2

Virus inactivation by means of BACI or Entozon at 45°C

5	Virus	Time	Substance Addition (mg/ml)	Virus titer found (log ₁₀ /ml)	Virus inactivation (log ₁₀ /ml)
10	BPV	1 hour	Control 0	4.7	0
			BACI 0.05	5.2	0
			" 0.01	5.2	0
		2 hours	Control 0	4.6	0
			BACI 0.05	4.6	0
			" 0.01	4.6	0
15		1 hour	Control 0	4.7	0
			Entozon 0.030	≤1.5	≥3.2
			" 0.015	≤1.5	≥3.2
		2 hours	Control 0	4.6	0
			Entozon 0.030	≤1.5	≥3.1
			" 0.015	≤1.5	≥3.1
20	PPV	1 hour	Control 0	5.6	0
			Entozon 0.030	3.3	2.3
			" 0.015	3.7	1.9
		2 hours	Control 0	5.6	0
			Entozon 0.030	2.2	3.4
			" 0.015	2.7	2.9

As the results in Table 2 show, BPV is not inactivated by BACI under the test conditions selected. Inactivation is possible by means of Entozon, inactivation with BPV taking place substantially more rapidly than with PPV.

Example 3

Virus inactivation by means of BACI and acriflavine

The suspensions of the virus species shown in Tab. 3 were treated with BACI or acriflavine and incubated at 37°C for 2 hours. Samples were then taken for titration to determine the virus inactivation.

Table 3

Virus	Substance addition (mg/ml)		Virus titer found (log ₁₀ /ml)	Virus inacti- vation (log ₁₀ /ml)
IBRV	Control	0	5.1	0
	BACI	0.01	≤1.5	≥3.6
	Acridflavine	0.001	1.8	3.3
PI ₃ V	Control	0	5.6	0
	BACI	0.01	≤1.5	≥4.1
	Acridflavine	0.001	3.2	2.4
BVDV	Control	0	6.2	0
	BACI	0.01	2.3	3.9
	Acridflavine	0.001	2.5	3.7
BPV	Control	0	5.4	0
	BACI	0.01	5.9	0
	Acridflavine	0.001	≤1.5	≥3.9

As the results in Table 3 show, the enveloped virus species - IBRV, PI₃V, BVDV - are inactivated both by BACI and acridflavine, the inactivation by BACI being somewhat greater. The naked virus BPV is inactivated by acridflavine, but not by BACI alone.

After virus inactivation by means of acridflavine and BACI was detected in EME medium, it was checked whether these substances can also inactivate virus in protein-containing solutions. The following protein solutions were treated with the virus species indicated:

20	Beriplex®	PPV
	Horse serum	BVDV, BPV
	Beriate®	BVDV, BPV, BAV-1, Reo 3, IBRV
	Haemate®	PPV, Reo 3
	Venimmun®	BVDV, PPV, CPV
25	FCS	CPV
	Egg allantoic fluid	Influenza A, Influenza B

The results obtained in these experiments are shown in tabular form below.

Example 4

Virus inactivation with acridines and benzalkonium chloride in protein solutions

5

As emerges from the results in Table 4, it is possible to inactivate completely different viruses in a methodologically simple manner in protein solutions using acridines and/or benzalkonium chloride. It appears clear here, however, that by means of benzalkonium chloride alone only envelope-containing viruses can be inactivated, whereas by means of acridines both envelope-containing and also nonenveloped virus species are inactivated. Both substances act synergistically in their virucidal action, i.e. the magnitude of the virus inactivation with the combination acriflavine + benzalkonium chloride is higher than with the two individual substances.

The results in Table 4 also show that virus inactivation in protein solutions is dependent on:

1. the virus species to be inactivated
2. the constituents and nature of the protein solution
3. the inactivating agent concentration
- 25 4. the inactivation time
5. the inactivation temperature.

The virus inactivation is also pH-dependent - results not shown. At a pH of below 5.5, virus inactivation takes place more slowly than at higher pHs.

30

Tables 5-7 contain the results of the biological activity of the protein solutions after virus inactivation by means of acriflavine and/or benzalkonium chloride. The biological activity was determined in Venimmun® by the content of antibodies before and after virus inactivation, and in Haemate®, Beriate® and Beriplex® by the determination of the clotting-promoting activity - measured in international units.

35

Table 4

Virus inactivation with acridines and benzalkonium chloride in protein solutions

Protein solution and virus	Inactivating agent	Concentration (mg/ml)	Inactivation Temperature (°C)	Inactivation time (h)	Control titer (\log_{10}/ml)	Treatment titer (\log_{10}/ml)	Titer reduction (\log_{10}/ml)
Horse serum + BPV	Acriflavine	0.001	37	0	5.4	5.4	0
				1	5.2	≤ 1.5	≥ 3.7
				2	5.1	≤ 1.5	≥ 3.6
Horse serum + BVDV	Acriflavine	0.001	37	0	5.0	5.0	0
				1	5.1	≤ 1.5	≥ 3.6
				2	5.0	≤ 1.5	≥ 3.5
Beriate + BPV	Acriflavine	0.001	37	0	5.4	5.4	0
				1	5.0	≤ 1.5	≥ 3.5
				2	5.0	≤ 1.5	≥ 3.5
Beriate + BVDV	Acriflavine	0.001	37	0	5.0	5.0	0
				1	5.0	≤ 1.5	≥ 3.5
				2	4.8	≤ 1.5	≥ 3.5
Beriate + Reo 3	Ethacridine lactate	0.3	45	0	5.4	5.1	0.3
				1	4.7	≤ 1.5	≥ 3.2
				2	4.7	≤ 1.5	≥ 3.2
Beriate + IBR	Ethacridine lactate	0.3	45	0	6.5	6.5	0
				1	5.7	2.0	3.7
				2	4.3	≤ 1.5	≥ 2.8

Table 4 (continued)

Virus inactivation with acridines and benzalkonium chloride in protein solutions

Protein solution and virus	Inactivating agent	Concentration (mg/ml)	Inactivation Temperature (°C)	Inactivation time (h)	Control titer (log ₁₀ /ml)	Treatment titer (log ₁₀ /ml)	Titer reduction (log ₁₀ /ml)
Haemate + PPV	Acriflavine	0.001	37	0	5.4	5.5	0
				1	5.5	3.3	2.2
				2	5.5	1.9	3.6
				3	5.3	≤1.5	≥3.8
Venimmun + PPV	Acriflavine	0.001	37	0	4.0	4.0	0
				1	3.9	≤1.5	≥2.4
				2	3.9	≤1.5	≥2.4
Venimmun + CPV	Acriflavine	0.001	37	0	6.9	6.6	0.5
				1	6.8	4.8	2.0
				2	6.8	3.9	2.9
				3	6.9	3.9	3.0
Venimmun + BVDV	Acriflavine	0.001	37	0	6.4	6.4	0
				1	5.8	4.5	1.3
				2	6.3	1.9	4.4
				3	6.0	0	≥6.0

Table 4 (continued)

Virus inactivation with acridines and benzalkonium chloride in protein solutions

Protein solution and virus	Inactivating agent	Concentration (mg/ml)	Inactivation temperature (°C)	Inactivation time (h)	Control titer (log ₁₀ /ml)	Treatment titer (log ₁₀ /ml)	Titer reduction (log ₁₀ /ml)
Egg allantoic fluid + Influenza virus B	Acriflavine	0.001	37	0	7.4	7.4	0
				1	7.1	6.4	0.7
				2	6.9	5.0	1.9
Egg allantoic fluid + Influenza virus B	BACI	0.02	37	0	7.4	7.4	0
				1	7.1	6.0	1.1
				2	6.9	3.6	3.3
Egg allantoic fluid + Influenza virus B	Acriflavine + BACI	0.001 0.02	37	0	7.4	7.4	0
				1	7.1	4.1	3.0
				2	6.9	2.5	4.4
Beriplex + PPV	Acriflavine	0.001	30	0	4.8	4.8	0
				1	4.6	3.6	1.0
				2	4.6	2.9	1.7
				3	4.8	≤1.5	≥3.3
Beriplex + PPV	BACI	0.001	30	0	4.8	4.8	0
				1	4.8	4.8	0
				2	4.6	4.8	0
				3	4.6	4.6	0
Beriate + PPV	Acriflavine + BACI	0.001 0.01	30	0	4.8	4.8	0
				1	4.8	3.5	1.3
				2	4.6	≤1.5	≥3.1
				3	4.6	≤1.5	≥3.1

Table 4 (continued)

Virus inactivation with acridines and benzalkonium chloride in protein solutions

Protein solution and virus	Inactivating agent	Concentration (mg/ml)	Inactivation Temperature (°C)	Inactivation time (h)	Control titer (log ₁₀ /ml)	Treatment titer (log ₁₀ /ml)	Titer reduction (log ₁₀ /ml)
Beriplex + PPV	Acriflavine	0.001	37	0	4.8	4.8	0
				1	4.6	2.0	2.6
				2	4.6	≤1.5	≥3.1
				3	4.8	≤1.5	≥3.3
Beriplex + PPV	BACI	0.01	37	0	4.8	4.8	0
				1	4.6	4.6	0
				2	4.6	4.6	0
				3	4.8	4.6	0.2
Beriplex + PPV	Acriflavine + BACI	0.001 0.01	37	0	4.8	4.8	0
				1	4.6	1.8	2.8
				2	4.6	≤1.5	≥3.1
				3	4.8	≤1.5	≥3.3
FCS + CPV	Acriflavine	0.001	37	0	6.6	6.6	0
				1	n.d.	4.9	1.7
				2	n.d.	4.0	2.6
				3	6.9	3.4	3.5
FCS + CPV	Acriflavine	0.001	45	0	6.8	6.8	0
				1	n.d.	4.8	2.0
				2	n.d.	3.5	3.3
				3	7.0	2.8	4.2

Table 5

Determination of the biological activity (antibody titer) in protein solutions before and after virus inactivation by means of acriflavine and benzalkonium chloride

5	Protein solution	Name	Temperature and duration of the treatment	Reciprocal neutralization titer ¹ against polio virus Type 1	
				Without inactivating agent	With inactivating agent ²
10	Low-cryo human plasma (individual plasma)	H1	37°C	646	646
		H2		741	562
		H3		741	646
		H4	2 hours	646	741
		H5		376	562
15	Venimmun® (Final product) various batches	V1	37°C	2234	851
		V2		1950	1698
		V3		1698	1698
		V4	2 hours	1698	1698
		V5		1479	1479
20	Low-cryo human plasma (individual plasma)	H1	45°C	427	977
		H2		1288	977
		H3		1288	977
		H4	2 hours	977	1122
		H5		977	1288
25	Venimmun® (Final product) various batches	V1	45°C	1950	2234
		V2		2570	2234
		V3		2234	1479
		V4	2 hours	2234	1950
		V5		2234	1479

¹ Titer calculation according to Spearman-Kärber from log₂ dilution series using 8 replicates/dilution stage

30 ² Acriflavine 0.001 mg/ml + BACI 0.02 mg/ml

Table 6

Determination of the biological activity (antibody titer)
in protein solutions before and after virus inactivation
by means of acriflavine and benzalkonium chloride

	Protein solution	Name	Temperature and duration of the treatment	Rec. HAH anti-PI, virus		Rec. HAH anti-rec3 virus	
				Antibody titer ¹		Antibody titer ¹	
				Without I. ²	With I. ²	Without I. ²	With I. ²
10	Low-cryo human plasma (individual plasma)	H1	45°C 2 hours	80	80	320	320
		H2		80	80	320	320
		H3		80	80	320	320
		H4		80	80	320	320
		H5		80	80	320	320
15	Venimmun® (Final product) various batches	V1	45°C 2 hours	320	320	320	320
		V2		320	320	320	320
		V3		320	320	320	320
		V4		320	320	320	320
		V5		320	320	320	320
20	Horse serum (individual sera)	P1	45°C 2 hours	n.d.	n.d.	640	640
		P2				640	640
		P3				640	640
		P4				640	640
		P5				640	640

¹ Titer determination in log₂ dilution series

² I. = inactivating agents: acriflavine 0.001 mg/ml + BACI 0.02 mg/ml

Table 7

Determination of the biological activity (clotting activity) of protein solutions before and after virus inactivation by means of acriflavine (A) and benzalkonium chloride (BACL)

	Protein solution	Temperature and duration of the treatment	Inactivating agent	Inactivating agent concentration (mg/ml)	Activity (IU/ml)
10	cryo-protein solution after Al(OH) ₃ + QAE treatment	3 hours 45°C	A	0.01	3.9
			A	0.03	4.2
			A	0.001	4.4
			BACI	0.1	6.9
15			BACI	0.05	6.1
			A + BACI	0.001 + 0.05	4.1
			Control	0	5.3
20	Haemate® Factor VIII	3 hours 37°C	A	0.002	18.9
			A	0.001	16.8
			BACI	0.02	20.7
			A + BACI	0.001 + 0.02	17.6
			Control	0	24.1
25	Beriplex® Factor II	3 hours 37°C	A	0.002	48.8
			A	0.001	50.0
			BACI	0.02	61.3
			A + BACI	0.001 + 0.02	47.9
			Control	0	68.6

As emerges from the results in Tables 5 and 6, the content of neutralizing (Polio Type 1) and hemagglutination-inhibiting (HAH) antibodies (PI₃- and Reo 3 virus) in Venimmun® is not

affected to an extent exceeding the test variations (as a rule ± 1 log₂ stage) during virus inactivation by means of acridines and benzalkonium chloride. The activity decrease with the clotting preparations (Beriate®,
5 Haemate®, Beriplex®) after acridines/benzalkonium chloride inactivation is tolerable (Table 7).

THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE
PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

- 5 1. A process for the inactivation of viruses, which
 comprises employing acridine or an acridine deriva-
 tive.
2. The process as claimed in claim 1, wherein benzal-
10 konium chloride is additionally employed.
3. The process as claimed in claim 1 or 2, which is
 carried out in the presence of proteins and wherein
 the biological activity of these proteins is
15 retained.
4. The process as claimed in claim 1, 2 or 3, wherein
 the incubation is carried out at a temperature of
 20-60°C.
- 20 5. The process as claimed in one of the preceding
 claims 1-4, wherein the temperature is 25-37°C.
6. The process as claimed in one of the preceding
25 claims 1-5, wherein the incubation is carried out at
 pH 5-9.
7. The process as claimed in one of the preceding
 claims 1-6, wherein acridine or the acridine deriv-
30 ative is employed in a concentration of 0.0001 to
 1.0 g/l.
8. The process as claimed in claim 7, wherein acridine
 or the acridine derivative is employed in a concen-
35 tration of 0.0005 to 0.1 g/l.
9. The process as claimed in one of the preceding
 claims 2-8, wherein benzalkonium chloride is emp-
 loyed in a concentration of 0.004 to 0.1 g/l.

10. The process as claimed in claim 9, wherein benzalkonium chloride is employed in a concentration of 0.001 to 0.05 g/l.
- 5 11. The process as claimed in one of the preceding claims 1-10, wherein the incubation time is 0.5 h - 10.0 h.
- 10 12. The process as claimed in claim 11, wherein the incubation time is 2-5 h.
13. The process as claimed in one of the preceding claims 1-12, wherein the viruses are parvoviruses or other nonenveloped viruses.
- 15 14. The process as claimed in one of the preceding claims 1-13, wherein the viruses are enveloped viruses.

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1994/B020 - Ma 1043

Abstract

Process for the inactivation of viruses with the aid of acridine or acridine derivatives

The invention relates to the use of acridine or acridine derivatives, preferably in combination with benzalkonium chloride, for the inactivation of enveloped or nonenveloped viruses. The process according to the invention is preferably carried out in the presence of proteins whose biological activity is substantially retained.